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Paper TT01

Disruption Leads to Innovation
Alexa for Clinical Research

Chris Decker, d-Wise, Morrisville, NC USA

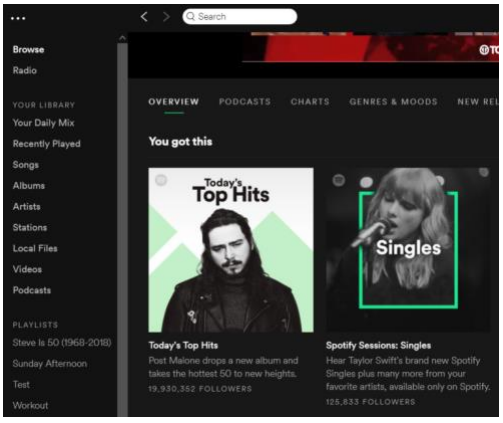
ABSTRACT

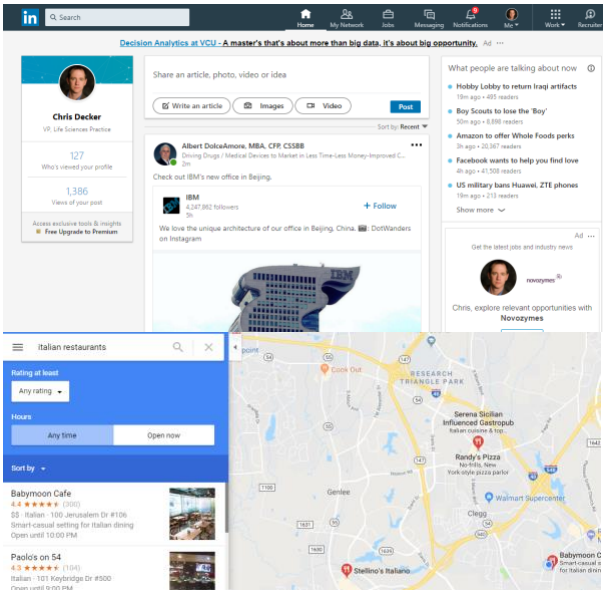
In our personal lives we live in a connected world we take for granted. We are connected through Facebook, Uber, and Alexa with answers at our fingertips. In our clinical trial universe, we still ask people to write stand along subjective specifications, others to write pages of code over many weeks, and yet others to confirm, check, and duplicate just to give us a single number.

If we step back from our what we do today, our current paradigm, how absurd is this? Where could we be in 5 years if we paused and said, "what if…"? Imagine a world where we have integrity and context embedded within the data, onerous and prescriptive manual steps are replaced by user experience and automation, and users gain insights from the data allowing machines to derive meaning. Does this sound like a bit of fantasy? Well, the reality is that other industries already do it and so can we! Within this presentation, we'll provide you insights into how we could ask Alexa for the answer in the future.

INTRODUCTION

In today's world we use various technologies so seamlessly that we take for granted how complex the plumbing is for those solutions. We listen to music from anywhere, find colleagues online, and can locate any kind of restaurant close by.





We use smart phones to text, take selfies, and find information – all of which seem simple. However, under the hood, the neural network of data that provides those capabilities is massive and uses robust technologies that bring that information to your fingertips. We should all be asking ourselves and exploring how we can have this same capability within our clinical data.

This paper will outline the top three roadblocks we face in moving towards a future allowing us to accelerate the work we do, have more confidence in our outputs, and gain true insights from our data. Then we will describe how we might take the steps to reach these lofty goals and initial conceptual ideas on how to get there.

CURRENT PARADIGM

At a high level, there are three fundamental challenges we face in today's paradigm that stifle our ability to innovate and put a ceiling on our ability to move forward.

SILOS LIMIT INNOVATION

"Silos build the wall in people's minds and create the barrier in organizations' hearts." PEARL ZHU

The first challenge we encounter is more of a people or culture issue then a technology challenge. Within our industry groups of people live in isolated silos producing many manual steps and throw artifacts over the wall with no context or understanding each other's needs just to get to the end of their process. Today, all the "intelligence" resides in people's heads. People are authoring documents or creating data in silos with no holistic view of the study or program and information is being duplicated and manually transferred from place to place. The wheel is being constantly reinvented. What does this all add up to? – inefficiency, perceived quality that isn't real, extended timelines and an overall façade that you are following a 'standard operating process'.

Many of these silos exist within our ecosystem. Within our own companies we throw things over the wall to each other without enough context. Between regulatory and industry, we create a wall of formality where we are overly cautious about sharing anything. And even with standards organizations the individual teams have evolved from a place of islands leading to disconnected and inconsistent standards.

BROKEN DATA PARADIGM

"In the real world, we want to capture the complexity and diversity of the standard of care without forcing it into an artificial structure. The current technology framework used within clinical trials to collect information often makes researchers constrain data to a structure that is not real and has no context…… and forces them into this rigid non-intuitive thought process" – Florence Barkats

Forty years ago, we started collecting and analyzing data using SAS and defined the SAS data set and transport format as the standard for interoperability and representing clinical information. It was the best choice at the time given what we had available. Unfortunately, it has now become our crutch and severely limits our ability to truly represent our data. The two dimensions below cause us to create more and more data, variables, and standalone siloed specification documents in an attempt to connect the information and put a band aid on a multi-dimensional problem.

Our two-dimensional data paradigm that we are so tied to is severely limiting and will never provide us the ability to automate and gain insights from our data no matter how many times we try.

We're drowning in an ocean of data without context and overflowing with disconnected documentation. Current data collection does not reflect patient care and is far-removed from the source. Data is collected and stored in disparate files, requiring constant monitoring, reviewing, and manual cleaning to ensure medical and scientific integrity. So much time is spent on specifications, data transformations, formatting of results, and validation rather than insight, leading to

prescriptive analysis lacking in scientific curiosity and discovery. We create single use data, analyses, and reports and then put them on a shelf struggling to get answers to simple questions.

20TH CENTURY TECHNOLOGY TO SOLVE 21ST CENTURY PROBLEMS

In our industry, we continue to solve problems today with technology from the last century. What does Windows 1.0, Nokia Talkman, the first Nintendo Entertainment System, and the first Macintosh computer have in common? They were all introduced circa 1985. You know what was also introduced in 1985? – the SAS transport file, a 'technology' that was the foundation of standards development and our core processes for the last 30+ years.

Now, this SAS format is just one example of the technology constraints we have put on ourselves. With the silos described earlier, we have led vendors to build solutions to support those silos, solutions that solve a siloed problem and don't usually integrate with the step before or the step after.

Not only do we not leverage current technology, but we also don't embrace current methodologies like design thinking, user experience, and agile. We pretend to do things in an 'agile' way but often we don't understand what that really means. Think about the app you love to use on your phone…now tell me an app you love to use in your day to day work.

How can we possibly maintain context and relationships in our information with these self-imposed, archaic limitations? We must fundamentally change our current data, people, and technology paradigm to have any chance of significantly helping patients.

WHERE COULD WE GO?

Let's start by saying that we don't have the golden ticket, the answer to solve world hunger, or the exact path forward to define how we fundamentally change. But we must start somewhere….and below are just a few ideas.

BRIDGE THE SILOS

Within our industry we all have our well-defined titles and responsibilities, and in those roles, someone gives you an input, you do your siloed job on that thing, and then throw it over the wall to the next person. What if were to change all our titles to "Data Scientist", we all had the same title and redirect our focus on doing a task with the mindset of helping the patient.

People use the phrase 'breaking down the silos' when referring to this issue. It's not about breaking down the silos but more about building a bridge; a firm, well architected bridge so that the people who specialize in their niche can do their work and clearly understand what they need from someone and what they need to give someone else.

Functions within Pharma must understand and care what their upstream and downstream customers need, but also must be given the technology and data framework to share that information. Pharma and regulators must not put up walls when discussing challenges…they must share each other's pains, frustrations, and truly collaborate. We have glimpses of this industry collaboration across various organization such as the PhUSE working groups, but we must do more of it.

Changing a decades old paradigm won't be easy, but we won't make progress if people keep holding on to tightly to their bit and don't look up to see what is going on around them. The first step is to agree that this is an issue and then clearly define what the bridges could look like.

CHANGING THE DATA PARADIGM

In our opinion, the most critical step is to understand that our data paradigm is fundamentally broken. As stated in the quote above from Florence Barkats, we "collect information that constrains the data to a structure that is not real and forces rigid non-intuitive thinking". Currently our paradigm follows a rigid process that removes all context from the data. We collect the data in two dimensions when clinical information is multi-dimensional, and we build isolated specifications that are not really connected to the data.

The first step is for everyone to understand that we must take the data out of two dimensions and co-locate the data and metadata. This is not something that is easy to do overnight but we must have everyone align and understand why this is so important. If we can all align on that concept, then we can start working on the same problem.

The picture below shows an example where we pulled apart a customer's standards and data and linked the information from the analysis backwards to the data collection point with both data and metadata. We were able prove this can be done.

The next step is to define how it can scale and support the variable processes we have within today's workflow. We must move toward a world that has contextual data if we are truly going to automate and gain insights from the data.

EMBRACE TECHNOLOGY

The final piece of the puzzle to innovation within our current paradigm forward is to fully embrace that we are squarely stuck in 20th century technology and we must invest time, people, and money into investigating and finding small wins for leveraging today's technology that will allow us to accelerate delivery and gain valuable insights from our data. In the short term, this transition will most likely be painful and we'll most likely be less efficient before we can be more efficient. But it's our commitment to patients that must make us force a path forward.

Recently, I discovered a website online that records my voice by reading 30 sentences. It processes this information, asks me to type in a sentence, and then reads that typed sentence back to me in my own voice. Wow! I know you are asking what this has to do with clinical research, and we won't discuss the ethical views of using artificial intelligence to mimic someone's voice. The key point is not the specific technology, but the fact that this advanced technology exists. Everyone needs to climb out of the box, expand your minds, and think about how technology like this could help us. What if a technology could listen to a physician and populate the EHR which flowed into my clinical data store without ever writing down a word? There are so many possibilities to what we could do if we really embraced the technologies that are available to us today. But let's get practical. Where do we start? How do we introduce these new capabilities while still maintaining a lot of our current process and infrastructure? How do we define a future and then build a bridge to get there?

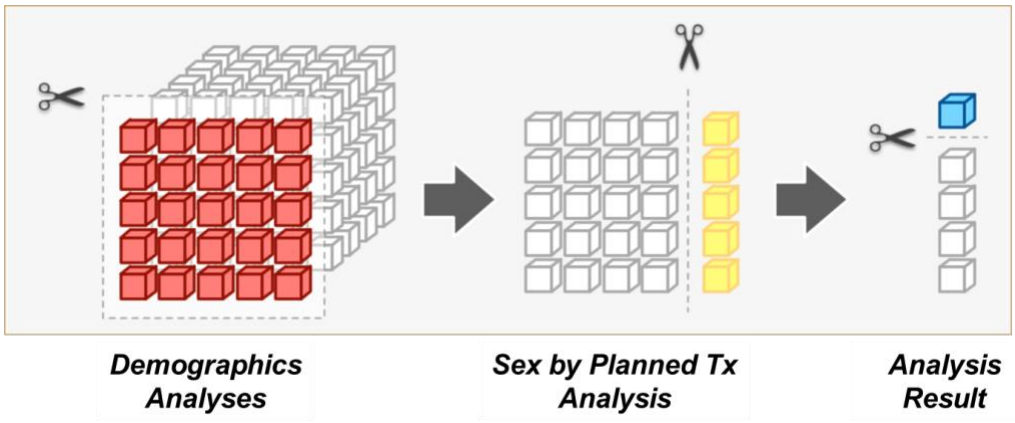
WHAT IF WE COULD DO THE FOLLOWING?

We must learn from history and use technologies to extract and learn from the plethora of artifacts that exist in our current environments – protocols, specifications, study reports – chocked full of information we can extract, curate, and reuse. We must look at steps in the data flow where we can plug in new capabilities enabling groups of people and making bits of the process more efficient.

We must look at technologies that fix the data paradigm and give us contextual data while still producing and potentially automating our standard artifacts such as SDTM and ADaM in the short term. In parallel, we must engage regulatory agencies to get them on board with submitting data in a structure that provides real traceability and ability to extract knowledge from the data.

WHAT IF WE COULD…STORE, CURATE, AND REUSE ANALYSIS RESULTS

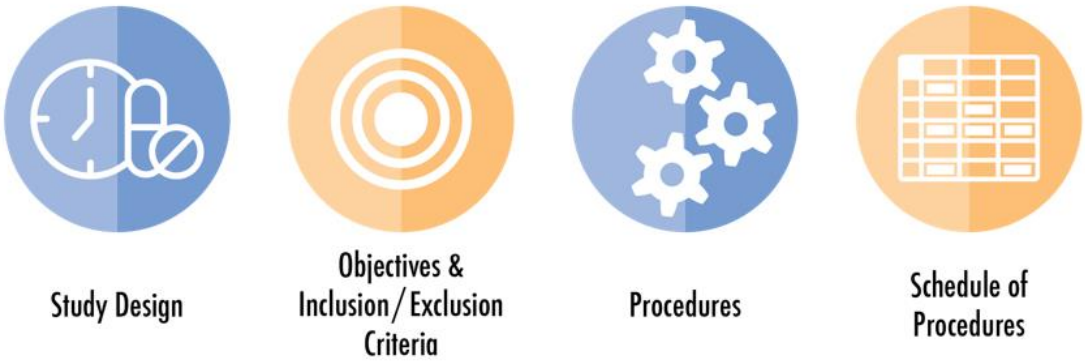
What if we could build a repository of analysis results that that can serve a breadth of different stakeholders instead of single use, throw away, paper tables and listings? This use case has been shown within a PhUSE working group and



with a number of our customers significantly reducing the number of programs and TFLs and providing traceability from the result to the data that supports it.

WHAT IF WE COULD….AUTOMAGICALLY EXTRACT USABLE CONTENT FROM THE PROTOCOL

What if a machine could read the contents of a protocol and extract study design information such as inclusion/exclusion criteria, objectives, and the schedule of events curating that information in a database and making it



searchable and usable to downstream processes? What if we could use that information to automatically pick the CRFs that are used for a study?

This can be done now through national language processing by identifying key components and letting the machines learn from many iterations of processing. We have worked with customers to tackle this concept within clinical study reports under the umbrella of clinical transparency and sharing of reports.

INTEGRATED SPECIFICATION

What if we could define our data standards in a way that truly links the information from the analysis through to how it was collected? This would require us to break down our current silos, take our content out of Excel spreadsheets and build a robust model which includes these relationships – contextual data. Again, this has been shown through PhUSE projects and working with our customers. In addition, CDISC is exploring the need to integrated across their standards as the next generation CDISC model.

CONCLUSION

As you read this paper, you might be either saying it's full of fairy tales that will never be realized, OR I like the ideas but struggle to understand where we start, OR this is where we need to go, let's charge the hill! No matter what you believe, I hope we can all agree that we find different ways to do our job, collect and analyze contextual data, and help get treatments to patients faster and with more confidence.

To achieve a new paradigm, it requires us to think in new ways and realize what our key unit of measure is – it's not a spreadsheet or a SDTM data set or a paper TFL. It's the analysis, the objective, the key clinical concept we are trying to capture and study. If we can shift our minds to think in a different way we can make major changes and disrupt the industry.

REFERENCES

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Clinical Trials as RDF: http://www.phusewiki.org/wiki/index.php?title=Clinical_Trials_Data_as_RDF

ACKNOWLEDGMENTS

I would like to acknowledge the small, but growing group of people across industry who continue to push these ideas forward. You know who you are and let's keep fighting the good fight.

RECOMMENDED READING

Linked Data 101: https://en.wikipedia.org/wiki/Linked_data
Moving to a Round World: https://www.lexjansen.com/phuse/2017/ds/DS10.pdf

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:

Chris Decker
d-Wise
919-995-0957
Chris.Decker@d-wise.com
www.d-wise.com